COMMITTEE UPDATE ON THE DEVELOPMENT OF FACTOR VIII AND VON WILLEBRAND FACTOR STANDARDS

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Development of Mega-2, a working standard for factor VIII activity

Supplies of Mega-1, the U.S. working standard for coagulation factor VIII are low. The Center for Biologics Evaluation and Research (CBER), FDA has, therefore, initiated efforts to replace the Mega-1 standard with Mega-2. Mega-2 is a plasma-derived factor VIII concentrate. It was selected based on the integrity of the factor VIII molecule, linearity of the dose-response over a wide range of concentrations, minimal inter- and intra-assay variability, stability of factor VIII potency over accelerated and long term storage, and consistent results between different test methodologies (e.g. one-stage APTT assay versus chromogenic substrate assay). The final fill of Mega-2 was performed in May 2000, and 100,000 vials will be available for distribution. At present, CBER/FDA is collaborating with the European Directorate for the Quality of Medicines and the National Institute for Biological Standards and Control (NIBSC) in organizing the final phase of the potency calibration for Mega-2. The standard is anticipated to be ready for distribution in year 2001.

Development of the first international standard for von Willebrand factor (vWF) concentrates

The development of the first international standard for vWF concentrates is a joint effort among CBER/FDA, NIBSC, and the Science and Standardization Committee (SSC) of the International Society on Thrombosis and Haemostasis. The initial characterization of five vWF concentrates was performed at three sites (CBER/FDA, NIBSC, and Laboratoire Francais du Fractionnement et des Biotechnologies). The results of the study were reported to the vWF subcommittee at the SSC annual meeting on June 16, 2000 in Maastricht, The Netherlands. The SSC has accepted the selection of two candidates for final phase of production and calibration. The two candidates were selected based on parallelism of dose-response curves, stability of preparations over accelerated and long term storage (i.e. stability of vWF multimers, antigen, and potency), similar results between different test methodologies (e.g. Ristocetin Cofactor Activity assay versus Collagen Binding assay), the ratio between activity and antigen, and the integrity of vWF multimers. A panel of 25-30 laboratories will be invited for the calibration studies. The final report of the study will be presented to the World Health Organization Expert Committee on Biological Standardization in October 2001.